Claims 1, 8-11, 13-24, 32-45 and 53-56 are pending in the application. Claims 2-7, 12, 25-31, 46, 47, 57 and 58 have been withdrawn from consideration by the Examiner as being non-elected. Claims 48-52 have been canceled previously, without prejudice to filing one or more divisional applications directed to the canceled subject matter thereof.

At pages 3-6 of the final Office Action, claims 1, 8-11, 13-24, 32-45 and 53-56 have been rejected under 35 U.S.C. §103(a) as obvious over US 5,846,966 ("Rosenblum et al.") in view of Belamarich et al. (Pediatrics, 1990; 86(6):977-81).

The Rejection

In the rejection, it is alleged that Rosenblum et al. disclose ezetimibe, with HMG-CoA reductase inhibitors such as simvastatin, are useful for reducing cholesterol and risk of atherosclerosis, as well as dosages for treating hypercholesterolemia. Final Office Action at page 3, lines 22-26.

It is acknowledged in the rejection that Rosenblum et al. do not expressly teach employing ezetimibe with simvastatin, an HMG-CoA reductase inhibitor and/or cholestyramine, in the dosage herein claimed to treat sitosterolemia. Final Office Action at page 4, lines 3-5.

It is further alleged in the rejection that Belamarich et al. teach that hypercholesterolemia is one of the manifestations of sitosterolemia and that cholestyramine and low sterol diet are effective at lowering both cholesterol and sterol levels in sitosterolemic patients. Final Office Action at page 4, lines 6-10.

In the rejection, it is stated that one of ordinary skill in the art would have been motivated to employ ezetimibe with simvastatin and/or cholestyramine to treat sitosterolemia because Rosenblum et al. teach the combination of ezetimibe and simvastatin to reduce cholesterol. Final Office Action at page 4, lines 11-16. It is alleged that employing the combination of ezetimibe and simvastatin in a method to reduce cholesterol and thereby treat sitosterolemia, a

condition known to have elevated cholesterol, would have been reasonably expected to be effective, absent evidence to the contrary. Final Office Action at page 4, lines 16-20. It is further alleged in the rejection that cholestyramine is known to be effective in lowering cholesterol in sitosterolemic patients and, therefore, administering all three compounds concommitantly for the same purpose would have been obvious to one of ordinary skill in the art, citing In re Kerkoven. Final Office Action at page 4, line 20 – page 5, line 1. Optimization of dosages and regimens is alleged in the rejection to be an optimization of result effect parameters. Final Office Action at page 5, lines 1-3.

In the section of the Final Office Action entitled "Response to Arguments", it is alleged that:

> Hidaka et al. teaches an HMG-CoA reductase inhibitor as effective in treating sitosterolemia [in] that it can reduce the plant sterol level in sitosterolemic patients. Therefore, employing HMG-CoA reductase inhibitor in a method of treating sitosterolemia along with other agents such as those herein claimed would be reasonably expected to be successful and effective.

Also, in the Final Office Action, Applicant's arguments with regard to long felt need were considered but not found persuasive because there was allegedly no showing that others of ordinary skill in the art were working on the problem and, if so, for how long. Final Office Action at page 5, lines 13-16. In the Final Office Action, it was alleged that there is no evidence that if persons skilled in the art who were presumably working on the problem knew of the teachings of the above cited references, they would still be unable to solve the problem. Final Office Action at page 5, lines 16-19.

In the Final Office Action, it is stated that Applicant's arguments averring certain types of sitosterolemic patients having normal cholesterol levels were considered, but not found persuasive since the arguments are drawn to an unclaimed limitation since the present claims do not exclude any types of sitosterolemic patients. Final Office Action at page 5, line 20 – page 6, line 2.

Also, in the Final Office Action it was stated that Applicant's arguments averring teaching away by Belamarich were considered, but not found persuasive "since HMG-CoA reductase inhibitors, such as pravastatin, was shown to be effective when using in combination with cholestyramine to treat sitosterolemia." Final Office Action at page 6, lines 3-6.

Discussion

Applicant respectfully traverses this rejection and requests that the rejection be reconsidered and withdrawn.

When making a rejection under 35 U.S.C. § 103, the Examiner has the burden of establishing a prima facie case of obviousness. In re Fritch, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). The Examiner can satisfy this burden only by showing an objective teaching in the prior art, or knowledge generally available to one of ordinary skill in the art, which would lead an individual to combine the relevant teachings of the references [and/or the knowledge] in the manner suggested by the Examiner. Id.; In re Fine, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988).

The mere fact that the prior art could be modified does not make the modification obvious *unless the prior art suggests the desirability of the modification* (emphasis added). In re Fritch, 23 U.S.P.Q.2d at 1784; In re Laskowski, 10 U.S.P.Q.2d 1397, 1398 (Fed. Cir. 1989); In re Gordon, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984).

"The ultimate determination of patentability must be based on consideration of the entire record, by a preponderance of evidence, with due consideration to the persuasiveness of any arguments and any secondary evidence." Manual of Patent Examining Procedure, (Rev. 1, Feb. 2003) § 716.01(d) and In re Oetiker, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992).